**Supplemental Tables**

**Supplemental Table 1 (Table S1): Disease categories and target genes in the NGS panel.**

|  |  |
| --- | --- |
| **Disease** | **Target genes** |
| ADPKD | *PKD1, PKD2* |
| ARPKD | *PKHD1* |
| NPHP | *NPHP1, INVS, NPHP3, NPHP4, IQCB1, CEP290, GLIS2, RPGRIP1L, NEK8, SDCCAG8, TMEM67, TTC21B, WDR19, ZNF423, CEP164, ANKS6, IFT172, CEP83, DCDC2, XPNPEP3, SLC41A1* |
| JBS | *NPHP1, CEP290, RPGRIP1L, TMEM67, TTC21B, ZNF423, CEP164, IFT172, INPP5E, TMEM216, AHI1, ARL13B, CC2D2A, OFD1, KIF7, TCTN1, TMEM237, CEP41, TMEM138, C5orf42, TCTN3, TMEM231, CSPP1, PDE6D, MKS1, TCTN2, B9D1* |
| MKS | *NPHP3, CEP290, RPGRIP1L, TMEM67, TMEM216, CC2D2A, TMEM231, MKS1, TCTN2, B9D1, B9D2* |
| SLS | *NPHP1, INVS, NPHP3, NPHP4, IQCB1, CEP290, GLIS2, SDCCAG8, WDR19, CEP164* |
| BBS | *CEP290, SDCCAG8, TMEM67, TTC21B, WDR19, IFT172, MKS1, BBS1, BBS2, ARL6, BBS4, BBS5, MKKS, BBS7, TTC8, BBS9, BBS10, TRIM32, BBS12, WDPCP, BBIP1, IFT27, CCDC28B* |
| IFT | *TTC21B, WDR19, IFT172, WDR35, IFT122, IFT140, IFT43* |
| ADTKD | *MUC1, UMOD, HNF1B* |
| Other | *ASS1, NOTCH2* |

ADPKD, autosomal-dominant polycystic kidney disease; ADTKD, autosomal-dominant tubulointerstitial kidney disease; ARPKD, autosomal-recessive polycystic kidney disease; BBS, Bardet-Biedl syndrome; IFT, intraflagellar transport; JBS, Joubert syndrome; MKS, Meckel syndrome; NPHP, nephronophthisis; SLS, Senior-Løken syndrome.

**Supplemental Table 2 (Table S2): Coverage of the *PKD1* and *PKD2* genes.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Average** | **95% confidence interval** | **Range** |
| *PKD1* (exons 2-46) |  |  |  |
| Mean depth | 714.0 | 518.4 to 909.6 | 341.8 to 1075.4 |
| Exon coverage (%) depth ≥5 | 100 | 100 | 100 |
| Exon coverage (%) depth ≥10 | 100 | 100 | 100 |
| Exon coverage (%) depth ≥20 | 100 | 100 | 100 |
|  |  |  |  |
| *PKD2* (all exons) |  |  |  |
| Mean depth | 431.3 | 298.5 to 564.2 | 159.0 to 645.8 |
| Exon coverage (%) depth ≥5 | 100 | 100 | 100 |
| Exon coverage (%) depth ≥10 | 100 | 100 | 100 |
| Exon coverage (%) depth ≥20 | 99.3 | 98.7 to 99.9 | 97.5 to 100 |

**Supplemental Table 3 (Table S3): Mutations in the *PKD1* truncating group.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient No. a | Mutation | Gene | Exon/  Intron | cDNA change b | Protein change | ADPKD Mutation Database | CADD | Polyphen | SIFT | ExAC | ToMMo | Previous  Reports |
| T7 | frameshift | *PKD1* | 42 | c.11692\_11693delTC | p.S3898fs | None | None | None | None | None | None | Novel |
| T19 | nonsense | *PKD1* | 43 | c.11816G>A | p.W3939\* | None | 52.0 | None | None | None | None | Novel |
| T38 | frameshift | *PKD1* | 23 | c.8631delC | p.N2878fs | None | None | None | None | None | None | Novel |
| T39 | nonsense | *PKD1* | 6 | c.1287G>A | p.W429\* | None | 27.7 | None | None | None | None | Novel |
| T55 | frameshift | *PKD1* | 42 | c.11569\_11572dupTACA | p.S3858fs | None | None | None | None | None | None | Novel |
| T65 | frameshift | *PKD1* | 15 | c.6733\_6740delATCCAGGC | p.I2245fs | None | None | None | None | None | None | Novel |
| T66 | nonsense | *PKD1* | 15 | c.6472C>T | p.Q2158\* | Definitely Pathogenic | 37 | None | None | None | None | [1-3] |
| T70 | nonsense | *PKD1* | 8 | c.1687C>T | p.Q563\* | Definitely Pathogenic | 36 | None | None | None | None | [4] |
| T74 | frameshift | *PKD1* | 15 | c.5316dupC | p.T1773fs | None | None | None | None | None | None | Novel |
| T100 | frameshift | *PKD1* | 8 | c.1669\_1670delCT | p.L557fs | None | None | None | None | None | None | Novel |

CADD, combined annotation-dependent depletion; SIFT, sorting intolerant from tolerant; ExAC, exome aggregation consortium;

ToMMo, Tohoku Medical Megabank Organization

a The patient No. was assigned by Toranomon Hospital

b NCBI reference sequences: *PKD1*, NM\_001009944.2

**Supplemental Table 4 (Table S4): Mutations in the *PKD1* non-truncating group.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient No. a | Mutation | Gene | Exon/  Intron | cDNA change b | Protein change | ADPKD  Mutation Database | CADD | Polyphen | SIFT | ExAC | ToMMo | Previous  reports |
| T5 | missense | *PKD1* | 38 | c.11102T>G | p.L3701R | None | 15.35 | 1.0 | None | None | None | Novel |
| T23 | missense | *PKD1* | 19 | c.7546C>T | p.R2516C | High Likely Pathogenic | 29.2 | 0.995 | None | None | None | [5] |
| T24 | missense | *PKD1* | 27 | c.9505C>T | p.R3169W | None | 27.8 | 0.773 | None | 1.66E-05 | None | Novel |
| T35 | missense | *PKD1* | 7 | c.1522T>G | p.C508G | None | 17.49 | 0.998 | None | None | None | Novel |
| T37 | missense | *PKD1* | 33 | c.10309C>G | p.L3437V | None | 10.44 | 0.354 | None | None | None | Novel |
| T49 | missense | *PKD1* | 42 | c.11614G>C | p.E3872Q | High Likely Pathogenic | 21.6 | 1 | None | None | None | [5,6] |
| T54 | missense | *PKD1* | 28 | c.9586T>A | p.F3196I | None | 12.52 | 0.926 | None | None | None | Novel |
| T56 | missense | *PKD1* | 15 | c.5770G>A | p.G1924S | None | 0.01 | 0.037 | None | 0.00013 | 0.0005 | Novel |
| T59 | missense | *PKD1* | 15 | c.6796C>G | p.R2266G | None | 14.1 | 1 | None | None | None | Novel |
| T64 | missense | *PKD1* | 17 | c.7117T>C | p.C2373R | None | 19.08 | 0.0 | 0.0 | None | None | Novel |
| T69 | UTR | *PKD1* | 5’UTR | c.-70\_-69dupGGGCCCC | － | None | None | None | None | None | None | Novel |
| T77 | missense | *PKD1* | 17 | c.7100C>T | p.S2367F | None | 17.32 | 0.006 | 0.03 | 0.00012 | None | [1] |
| T78 | missense | *PKD1* | 18 | c.7381G>C | p.A2461P | None | 26.2 | 0.996 | None | None | None | Novel |
| T84 | missense | *PKD1* | 15 | c.3416T>A | p.V1139E | None | 12.62 | 0.962 | None | None | None | Novel |
| T95 | missense | *PKD1* | 22 | c.8087T>G | p.L2696R | None | 0.35 | 0.0 | None | 0.00047 | None | Novel |
| T115 | missense | *PKD1* | 15 | c.6643C>T | p.R2215W | Likely Pathogenic | 22.4 | 0.717 | None | 8.367E-06 | None | [5,7] |
| T116 | missense | *PKD1* | 5 | c.542T>A | p.V181D | None | 6.35 | 0.811 | None | None | None | Novel |

CADD, combined annotation-dependent depletion; SIFT, sorting intolerant from tolerant; ExAC, exome aggregation consortium;

ToMMo, Tohoku Medical Megabank Organization

a The patient No. was assigned by Toranomon Hospital

b NCBI reference sequences: *PKD1*, NM\_001009944.

**Supplemental Table 5 (Table S5): Mutations in the *PKD2* group.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient No. a | Mutation | Gene | Exon/  Intron | cDNA change b | Protein change | ADPKD  Mutation Database | CADD | Polyphen | SIFT | ExAC | ToMMo | Previous  reports |
| T8 | missense | *PKD2* | 15 | c.2819G>A | p.R940H | None | 12.46 | 0.001 | 0.11 | None | 0.0022 | Novel |
| T26 | missense | *PKD2* | 14 | c.2668G>A | p.E890K | None | 27.0 | 0.781 | 0.07 | 4.94E-05 | 0.0049 | [8] |
| T30 | nonsense | *PKD2* | 5 | c.1249C>T | p.R417\* | Definitely Pathogenic | 36.0 | None | None | None | None | [9] |
| T31 | nonsense | *PKD2* | 1 | c.239C>A | p.S80\* | None | 28.1 | None | None | None | None | Novel |
| T68 | frameshift | *PKD2* | 13 | c.2384delC | p.S795fs | None | None | None | None | None | None | Novel |
| T82 | nonsense | *PKD2* | 4 | c.878G>A | p.W293\* | None | 31.0 | None | None | None | None | Novel |
| T86 | frameshift | *PKD2* | 11 | c.2159dupA | p.N720fs | Definitely Pathogenic | 12.62 | 0.962 | None | None | None | [10] |
| T92 | frameshift | *PKD2* | 1 | c.420delG | p.G143fs | None | None | None | None | None | None | Novel |
| T94 | frameshift | *PKD2* | 11 | c.2159dupA | p.N720fs | Definitely Pathogenic | None | None | None | None | None | [10] |

CADD, combined annotation-dependent depletion; SIFT, sorting intolerant from tolerant; ExAC, exome aggregation consortium;

ToMMo, Tohoku Medical Megabank Organization

a The patient No. was assigned by Toranomon Hospital

b NCBI reference sequences: *PKD2*, NM\_000279.3

**Supplemental Table 6 (Table S6): Pathogenic mutations in the Other group.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient No. a | Mutation | Gene | cDNA change b | Protein change | CADD | Polyphen | SIFT | ExAC | ToMMo | Previous  Reports |
| T1 | missense  missense | *NPHP4*  *NPHP4* | c.2198G>A  c.2717G>A | p.G733D  p.R906H | 20.1  5.89 | 1  0.003 | 0  0.21 | 9.10E-05  0.00022 | 0.0037  0.0061 | Novel  Novel |
| T2 | missense  missense | *PKHD1*  *PKHD1* | c.1396G>A  c.1160A>T | p.G466R  p.N387I | 20.1  23.4 | 0.999  1 | 0.01  0 | None  None | None  None | [11]  Novel |
| T16 | frameshift | *OFD1* | c.505\_506delAG | p.D170fs | 24.0 | None | None | None | None | Novel |

CADD, combined annotation-dependent depletion; SIFT, sorting intolerant from tolerant; ExAC, exome aggregation consortium;

ToMMo, Tohoku Medical Megabank Organization

a The patient No. was assigned by Toranomon Hospital

b NCBI reference sequences: *NPHP4*, NM\_015102.4; *PKHD1*, NM\_138694.3; *OFD1*, NM\_003611.2

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